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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,560	06/04/2001	Christopher M. Dobson	720797.90019	3009

7590 07/21/2005

Carl R Schwartz
Quarles & Brady
Suite 2040
411 East Wisconsin Avenue
Milwaukee, WI 53202-4497

EXAMINER	
EMCH, GREGORY S	
ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 07/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,560	DOBSON, CHRISTOPHER M.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *May 31,2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-47,49,50 and 55-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-47,49,50 and 55-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claim 54 was canceled, claims 38, 40, 55, and 60 were amended, and new claim 61 was added in the communication dated May 31, 2005. Claims 38-47, 49, 50, and 55-61 are pending and under consideration. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The enablement rejection of claims 38-47, 49, 50, and 55-60 under 35 U.S.C. 112, first paragraph, are maintained for reasons of record in the office action dated February 4, 2005. Further, claim 61 is newly rejected for the reasons stated in said office action.

Applicant argues that claim 38 is now amended to specify that the solution be "in a state such that the protein is at least partially denatured, but self-association of the

protein can still occur." Applicant asserts that this concept finds support in, among other places, paragraph [0025] of the original application. Also, Applicant asserts that a balance between denaturing and self-association of the protein may be achieved by someone with a standard level of skill in the art simply by varying a few basic conditions such as protein concentration, ionic strength, and pH. Applicant asserts that there would be no undue burden here.

Applicant's argument has been fully considered and is not found to be persuasive. The specification at p. 5, lines 3-22 teaches a plurality of variations to the solution conditions, including alcohol concentration from 5 to 40% v/v, aliphatic nitrile concentration from 5 to 95% v/v, protein concentration is not limited in any way but it may be from 0.1mM to 10mM, and pH from 0.5 to 6.5, and temperature ranging from 0°C to 100°C. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The amended limitation to claim 38 does not negate the previous office action's assertion that reasonable detail is missing from the specification to enable members of the public to understand and carry out the invention. The claims do disclose no specific starting materials for the solution, no definitive steps, no temperature, no pH, and no conclusion.

Applicant argues that the specification provides sufficient guidance on how to make amyloid fibrils from any given protein. However, in the instant case the specification only contains suggestion on how to experiment to make amyloid fibrils from any given protein. The specification does not disclose the critical solution

conditions necessary to maintain function of forming a fibril. As stated in the previous office action dated February 4, 2005 (p.6, lines 17-19) Guijarro et al. (1998) teaches that "Proteins known to form amyloid fibrils *in vivo* have no obvious sequence or structural similarities, and where the soluble folds of the amyloidogenic precursors are known they span the range of secondary, tertiary, and quaternary structural elements." Therefore, the specification does not disclose the correlation between the structure (sequence) of the proteins encompassed by the invention and the function forming a fibril. Since detailed information regarding the structural and functional requirements of the peptides in the instant methods are lacking, it is unpredictable as to which encoding variations, if any, meet the limitations of the claims. Therefore, it would require undue experimentation by one of skill in the art to practice the invention as claimed without further guidance from the instant specification. It is again noted that Applicant has provided examples in the specification but not explained in which manner it may be extrapolated to apply to any given protein.

The rejection of claims 38-47, 49, 50, and 55-60 under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one of skill in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention are maintained for reasons of record in the office action dated February 4, 2005. Further, claim 61 is newly rejected for the reasons stated in said office action.

Applicant asserts that "with respect to the written description issue, the amended claim language was confirmed at paragraph [0025] containing the following sentence, "In the case of naturally occurring proteins conditions are typically chosen to denature at least partially the protein whilst retaining conditions in which self-association can occur." This statement finds its support in the solution conditions mentioned above (alcohol concentration from 5 to 40% v/v, aliphatic nitrile concentration from 5 to 95% v/v, protein concentration is not limited in any way but it may be from 0.1mM to 10mM, and pH from 0.5 to 6.5, and temperature ranging from 0°C to 100°C).

Applicant's argument has been fully considered and is not found to be persuasive for the reasons stated in the previous office action dated February 4, 2005. However, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Applicant has only provided evidence to practice the embodiments cited in p. 10, paragraph 24 of the previous office action, and thus has not provided adequate written description and evidence of possession of a claimed genus. As discussed in the previous office action, at p. 10, paragraph 25, the only factor present in the claims is a desired end product. The specification does not identify any particular portion of the

method that must be conserved, nor does it provide a disclosure of structure/function correlation. As stated previously, the art teaches that "proteins known to form amyloid fibrils *in vivo* have no obvious sequence or structural similarities, and where the soluble folds of the amyloidogenic precursors are known they span the range of secondary, tertiary, and quaternary structural elements." Accordingly, the supporting statement "in the case of naturally occurring proteins conditions are typically chosen to denature at least partially the protein whilst retaining conditions in which self-association can occur" in the specification does not provide adequate written description of the claimed genus.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 38 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps is maintained for reasons of record in the office action dated February 4, 2005. Applicant argues that claim 38 is now amended to specify that the solution be "in a state such that the protein is at least partially denatured, but self-association of the protein can still occur," and that this amendment addresses this concern.

Applicant's argument has been fully considered and is not found to be persuasive for the reasons stated in the previous office action dated February 4, 2005 (see pp.12-13 paragraphs 31 and 32). This amendment and the supporting disclosure in the specification (p. 5, lines 3-22) do not supply the omitted essential steps because the

claim does not "set out and circumscribe a particular area wit h a reasonable degree of precision and particularity and make clear what subject matter" it encompasses, "as well as make clear subject matter from which others would be precluded." (See Ex parte Erlich 3 USPQ2d 1011, at p. 1011 (Bd. Of Pat. App. And Inter. 1987). These conditions still have not been met by Applicant in instant claim 38.

Claims 38-47, 49, 50, 55-59, and 61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 38 recites the limitation "the non-naturally occurring fibril." There is insufficient antecedent basis for this limitation in the claim since the term "non-naturally occurring fibril" is not recited in any previous claim(s).

Claim Rejections - 35 USC § 102

The rejection of claims 38-40, 43-44, 47, 55, 56, and 60 under 35 U.S.C. 102b as anticipated by Jarrett & Lansbury (1992) are maintained for reasons of record in the office action dated February 4, 2005 (see pp.13-14, paragraphs 33-35).

The previous office action asserted that the Jarrett & Lansbury reference teaches methods with three proteins, OsmB, OsmG3, and OsmA, all of which form myloid fibrils, none of which occur naturally as they are all transmembrane proteins thus meeting the limitations of claims 38 and 60. Applicant argues that the cited reference does not

teach the amended claim language. Further, Applicant asserts that Jarrett & Lansbury did not report that "the ability to form amyloid fibrils was common to all proteins, and this is not suggested anywhere in this document," and that the reference uses non-naturally occurring peptides, i.e., peptide corresponding to residues 28-44 of the OsmB protein. Applicant asserts that at the "normal" function or location of that protein has no bearing on it's potential to form amyloid fibrils and that the deposits formed from β protein are characteristic of Alzheimer's disease.

Applicant's arguments have been fully considered and are not found to be persuasive. The Examiner agrees that the Jarrett & Lansbury reference did not teach the ability to form fibrils was common to all proteins; however, the claim language recites methods involving "a solution comprising a protein." The proteins recited in the methods of the Jarrett & Lansbury reference fall within the scope of the claims because the claims recite methods using a protein (including amyloidogenic proteins). Further, the limitation of "said solution being a state such that the protein is at least partially denatured but self-association of the protein can still occur" finds its support in the specification at paragraph [0025] and at p. 5, lines 3-22 (alcohol concentration from 5 to 40% v/v, aliphatic nitrile concentration from 5 to 95% v/v, protein concentration is not limited in any way but it may be from 0.1mM to 10mM, and pH from 0.5 to 6.5, and temperature ranging from 0°C to 100°C). The Examiner agrees that the destination of a protein has no bearing on it's potential to form naturally occurring amyloid fibrils. However, according to Applicant's own argument, the reference teaches methods using non-naturally occurring peptides. Hence, fibrils formed from these peptides would also

be non-naturally occurring. Thus, the methods taught by the Jarrett & Lansbury reference anticipate all of the limitations of the claims as stated in the previous office action dated February 4, 2005 (see pp.13-14, paragraphs 33-35).

The rejection of claims 38, 42, 44, 45, 46, 49, 55, 59, and 60 under 35 U.S.C. 102b as anticipated by Kedar et al. (1072) are maintained for reasons of record in the office action dated February 4, 2005 (see pp.14-15, paragraphs 37-39).

Applicant argues that the present invention is directed to processes that result in the production of amyloid fibrils that do not occur naturally and that the present invention does not encompass the natural formation of amyloid fibrils *in vivo* or methods of forming *in vitro* the same fibrils, which can be formed *in vivo*. Applicant asserts that this is different from the methods taught by Kedar et al. because said methods describe *in vitro* synthesis of amyloid fibrils from specific hormones, including calcitonin and insulin, both of which are known to form amyloid fibrils *in vivo*.

Applicant's argument has been fully considered and is not found to be persuasive. Kedar et al. teaches methods using bovine crystalline zinc insulin (p. 1137, second paragraph), not naturally occurring insulin. Hence, the reference teaches methods where both naturally and non-naturally occurring fibrils are formed. Thus, the methods taught by Kedar et al. anticipate all of the limitations of the claims.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached on Monday through Friday from 8:30AM to 5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gregory S. Emch, Ph. D.
Patent Examiner
Art Unit 1649
July 18, 2005

JOSEPH MURPHY
PATENT EXAMINER